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Crural Index and extensive atherosclerosis of crural vessels are associated with long-term cardiovascular mortality in patients with symptomatic peripheral artery disease

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ABSTRACT

Background and aims: Limited data exist on the association of the anatomical distribution of atherosclerotic lesions and the extent of atherosclerosis at defined arterial segments with life expectancy. We recently presented a new classification of the extent of atherosclerosis in crural vessels and showed that Crural Index (CIx) was associated with mid-term survival of symptomatic peripheral artery disease (PAD) patients. This study evaluates the significance of the extent of crural atherosclerosis on long-term cardiovascular mortality.

Methods: 887 consecutive patients with PAD, admitted for digital subtraction angiography (DSA) at Turku University Hospital Department of Vascular Surgery (Turku, Finland) between January 1st, 2009 and July 30th, 2011, were retrospectively analysed. Each crural angiographic image was graded according to CIx criteria. Aorto-iliac and femoro-popliteal arterial segments were similarly graded according to modified TASC II criteria. CIx was used as the categorical variable for the extent of atherosclerosis in crural vessels for survival analysis. Survival was also evaluated with respect to which arterial segment was most severely affected. Causes of death were provided by the Cause of Death Registry of Statistics Finland, updated on January 23rd, 2017.

Results: Altogether, 408 (46%) patients died during follow-up. The majority of deaths were due to cardiovascular causes (n = 246, 60%). Cardiovascular mortality was strongly associated with a high CIx (CIx III (Hazard ratio (HR) 2.16, Confidence interval (CI) 95% 1.23–3.80, $p = 0.007$)) and CIx IV (HR 3.513, 95% CI 1.93–4.565, $p < 0.001$), as compared to CIx 0. In patients having the crural segment as the most severely affected arterial segment, cardiovascular mortality was significantly increased (HR 2.321, 95% CI 1.45–3.73, $p < 0.001$), as was overall mortality (HR 2.177, 95% CI 1.53–3.10, $p < 0.001$).

Conclusions: High Crural Index and extensive crural vessel atherosclerosis are associated with long-term cardiovascular mortality, and both may serve as useful indicators of survival among patients with symptomatic PAD.

1. Introduction

Cardiovascular disease is the most important causes of morbidity and mortality in western countries. Patients with peripheral artery disease (PAD) appear to have the heaviest cardiovascular disease burden [1,2]. The prevalence of PAD has increased within all age groups during the past 20 years [3].

With diagnosed large vessel PAD, life expectancy is shorter than without diagnosis [4,5]. Furthermore, widespread atherosclerosis of lower extremity arteries is associated with a higher mortality compared to that of atherosclerosis localised to other vascular beds

Abbreviations: ABI, ankle brachial index; AFS, amputation free survival; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CIx, Crural index; CVD, cerebrovascular disease; DSA, digital subtraction angiography; ERDS, end-stage renal disease; MACCE, major adverse cardiovascular and cerebrovascular events; PAD, peripheral arterial disease; TASC, *Trans*-Atlantic Inter-Society Consensus; WIfI, Wound, Ischemia, and foot Infection.

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[2]. Studies have reported the predictive value of the ankle-brachial index (ABI) in atherosclerosis [1,2]. In addition to ABI, there are very few clinical indicators to assess PAD outcome [6,7]. The relationship of mortality with the extent of atherosclerosis at different vascular segments of the lower limb has not been thoroughly investigated.

The need for new methods of risk assessment of PAD patients has been emphasised [8]. The most widely used classification describing the extent and severity of atherosclerotic lesions is shown in the TASC [9] and TASC II [10,11] recommendations, which aim to guide decision making in everyday practice. Additional classifications of the severity and distribution of occlusive arterial lesions in the lower extremity have been characterised [12,13], but none of these have been shown to have predictive value regarding patient outcome, and they are not widely used in clinical practice. A runoff score of lower limb arteries has recently been characterised and has been shown to associate with patient outcome and cardiovascular events in revascularised patients [14]. These observations strongly suggest that the extent of atherosclerosis detected in digital subtraction angiography (DSA) may be applied as an indicator for patient outcome [15,16]. We have recently published a simple tool to measure the extent of crural vessel atherosclerosis, the Crural Index (CIx) [17,18]. High CIx and severe crural artery disease are associated with increased mid-term overall mortality and poor amputation-free survival, whereas lesions in the aorto-iliac or femoro-popliteal regions, classified in a similar manner adopted from the TASC II recommendations, do not comparably affect outcome [17,18]. The present study aims to further elucidate the significance of this finding regarding long-term overall and cardiovascular mortality with a follow-up time of up to 7 years. The TASC II classification for proximal lesions and CIx for crural lesions were analysed, as well as outcome with respect to the most severely diseased arterial segment.

2. Materials and methods

2.1. Patient cohort

887 consecutive patients, admitted at the Department of Vascular Surgery at the Turku University Hospital, either for diagnostic DSA or endovascular treatment of PAD, from January 1st, 2009 to July 30th, 2011, were retrospectively analysed. All patients were of Caucasian origin and were included regardless of the earlier treatment history. Both elective and urgent patients were recruited. During recruitment, DSA was the gold standard for imaging of atherosclerotic lesions in lower limb arteries at our department. DSA images from the clinically more severely affected lower limb were analysed. When both limbs met the criteria for critical limb ischemia or were otherwise symptomatic, the limb with the lowest average toe pressure was considered worse and entered into the study. In case of repeated DSAs during the recruitment period, only the first examination was analysed and taken into statistical analyses. The study was approved by the Ethical Committee of the Hospital District of South-Western Finland.

Baseline characteristics were retrospectively collected from Turku University Hospital electronic patient records, as described in an earlier publication by Jalkanen et al. [18]. Only ICD-10 coded diagnoses were registered. Risk factors were collected as follows; coronary artery disease (CAD), cerebrovascular disease (CVD), hypertension, active smoking, diabetes, sleep apnoea, chronic obstructive pulmonary disease (COPD), end-stage renal disease (ESRD), dyslipidaemia, ankle-brachial index (ABI), ankle pressure, toe-brachial index (TBI), toe pressure, revascularisation modality and medical treatment (anticoagulant, antithrombotic and statin). The Rutherford classification [19] for clinical severity of PAD was determined from patient files to assess the severity of ischemia. The date and official cause of death were provided by the Cause of Death Registry of Statistics, Finland, on January 23rd, 2017. As the Registry has a one-year delay registering official causes of death, conclusive follow-up data for the cohort, including both the date and official cause of death, was available for analysis until 31.12.2015, which was considered the cut-off point for follow-up.

2.2. DSA analysis

All DSA images were analysed by the corresponding author. The crural vessels were first analysed separately and each vessel coded as follows: no detectable occlusion or minor stenosis: 0; total occlusion less than 5 cm: 1; total occlusion less than 10 cm: 2; total occlusion less than 15 cm: 3; total occlusion more than 15 cm: 4. The Crural Index was created by the sum of the codes for all three individual crural vessels. If the sum was 0, the Crural Index was 0; for sums 1–3, the Crural Index was I; for sums 4–6, the Crural Index was II; for sums 7–9, the Crural Index was III; and for sums 10–12, the Crural Index was IV.

Aorto-iliac and femoro-popliteal segments were classified as described in TASC II [10,11]. Categorical variables for aorto-iliac and femoro-popliteal segments (TASC II classification A-D) were coded as follows; no disease: 0; TASC II A: 1; TASC II B: 2; TASC II C: 3; TASC II D: 4.

To assess the prognostic effects of lesion distribution in different arterial segments, each patient was assigned to a group of predominant disease localisation: 1) aorto-iliac, 2) femoro-popliteal and 3) crural, based on which 0–4 rating gave the highest score. If, for example, according to the TASC II classification, a patient had proximal lesions of grade 0–2, but a Crural Index of III, the patient was assigned to the crural group. If, however, the highest grade was equal in two or even three localisations, the patient was assigned to the group of the more proximal lesion with a similar score.

2.3. Statistical analyses

All statistical analyses were performed using the IBM SPSS version 22 statistics program. Categorical variables were expressed as frequency and percentage. For continuous variables, patient characteristics were expressed as mean ± either standard deviation (SD) or standard error (SE). Normal distribution was assessed with Shapiro-Wilk tests. Survival analyses were assessed by Kaplan-Meier curves and Log-rank statistics. A Cox regression analysis was performed to assess the final predictive value of factors affecting survival. Factors with $p < 0.2$ in Cox univariate analysis were forced into a Cox proportional hazard model. Multivariate analysis was carried out to assess the risk of death. $p < 0.05$ was considered statistically significant.

3. Results

3.1. Patient characteristics

Altogether, 408 (46%) patients died during follow-up. The distribution of causes of death in the study cohort and in the general Finnish population aged >65 years is shown in Fig. 1. Mean age of patients entering the study was 72.4 years, ranging from 40 to 98 years, and mean age at the end of follow-up was 76.3 years, ranging from 43 to 98 years. Table 1 shows the causes of death for each group of CIx and Table 2 for each group of the most severely diseased arterial segment.

3.2. Survival and extent and distribution of atherosclerosis

A four-grade classification of the extent of atherosclerotic

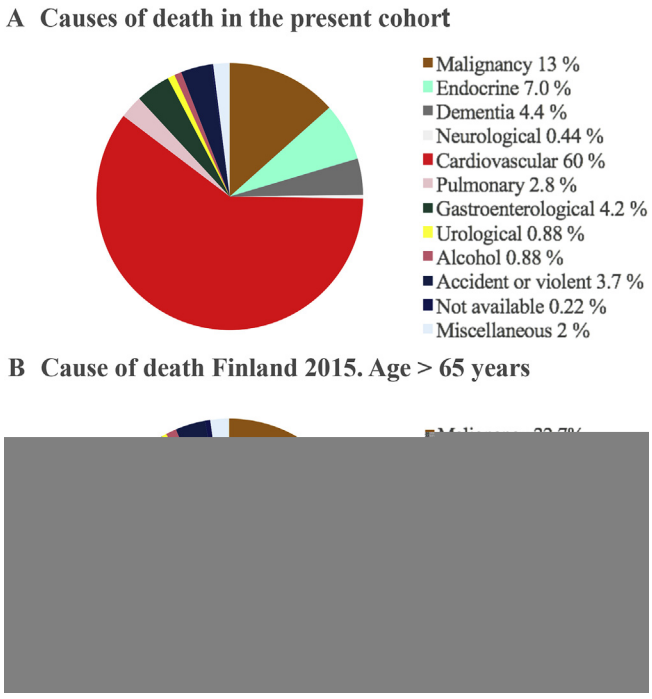

Fig. 1. Causes of death.
(A) In the study cohort, (B) in the Finnish population, age > 65 years. Finnish Centre of Statistics (Source ISSN = 1799–5051. 2015; http://www.stat.fi/til/ksyyt/ksyyt_2006-10-26_uut_001.html).

lesions was used for survival analyses. Segments were graded as described in the Materials and methods section. Crural Index III was associated with significantly shorter estimated cardiovascular survival than CIx grades 0, I and II ($p < 0.001$). Cardiovascular survival for CIx IV was significantly shorter compared to all other grades ($p < 0.001$ for CI 0-II and $p = 0.003$ for CI III). Kaplan-Meier survival curves for cardiovascular survival of CIx 0-IV are illustrated in Fig. 2A. CIx III was associated with significantly shorter estimated overall survival compared to grades 0, I and II ($p < 0.001$, $p = 0.002$ and $p < 0.001$, respectively) and CI IV was associated with significantly shorter estimated overall survival compared to all other grades ($p < 0.001$). Kaplan-Meier survival curves for overall survival for CIx 0-IV are shown in Fig. 2B.

No significant differences in overall survival were found between different grades of femoro-popliteal or aorto-iliac disease (data not shown).

Table 2
Causes of death by arterial segment most affected by atherosclerosis.

	Aorto-iliac	Femoro-popliteal	Crural	Total
Malignancy	9 (21%)	29 (18%)	16 (7.7%)	54 (13%)
Endocrine	0 (0%)	4 (2.5%)	25 (12%)	30 (7.4%)
Dementia	1 (2.3%)	4 (2.5%)	13 (6.3%)	18 (4.4%)
Neurological	1 (2.3%)	0 (0%)	1 (0.48%)	2 (0.49%)
Cardiovascular	23 (53%)	90 (56%)	132 (63%)	246 (60%)
Pulmonary	4 (9.3%)	6 (3.8%)	3 (1.4%)	13 (3.2%)
Gastroenterological	2 (4.7%)	9 (5.6%)	4 (1.9%)	15 (3.6%)
Urological	0 (0%)	2 (1.3%)	1 (0.48%)	3 (0.73)
Alcohol	1 (2.3%)	2 (1.3%)	1 (0.48%)	4 (0.97%)
Accident or violent	1 (2.3%)	8 (5.0%)	7 (3.4%)	16 (3.9%)
Not available	0 (0%)	1 (0.63%)	0 (0%)	1 (0.25%)
Miscellaneous	0 (0%)	4 (2.5%)	3 (1.4%)	7 (1.7%)
Death	42 (30%)	159 (38%)	206 (63%)	408 (46%)
Survived	98 (70)	257 (62%)	121 (37%)	479 (64%)
Total	141	417	329	887

Distribution of causes of death varied significantly between arterial segments for endocrine ($p < 0.001$), dementia-related ($p = 0.035$) and cardiovascular ($p < 0.001$) causes of death.

Analysis by the most severely diseased arterial segment revealed that the cohort with severe crural disease had a significantly shorter cardiovascular ($p < 0.001$) and overall ($p < 0.001$) mean estimated survival compared to the groups with predominantly femoro-popliteal or aorto-iliac disease (Fig. 3A and B). Both cardiovascular and overall mean estimated survival was significantly ($p = 0.046$ and $p = 0.015$, respectively) shorter in patients with femoro-popliteal disease than in patients with aorto-iliac disease.

3.3. Baseline factors affecting mortality

According to the significance in univariate analysis, the following variables were forced into Cox regression analysis for risk of cardiovascular mortality; age ($p < 0.001$), CAD ($p < 0.001$), hypertension ($p = 0.063$), diabetes ($p = 0.001$), COPD ($p = 0.046$), renal insufficiency ($p = 0.105$), hyperlipidaemia ($p = 0.089$), smoking history ($p < 0.001$), ABI ($p = 0.011$) and TBI ($p < 0.001$). Correspondingly, variables forced into Cox regression analysis for overall mortality were age ($p = 0.136$), CAD ($p = 0.002$), CVD ($p = 0.183$), hypertension ($p = 0.110$) diabetes ($p = 0.001$), renal insufficiency ($p < 0.001$), hyperlipidaemia ($p = 0.019$), smoking history ($p < 0.001$), ABI ($p = 0.003$) and TBI ($p < 0.001$).

3.4. Crural Index and mortality

For cardiovascular mortality, CIx III (Hazard ratio (HR) 2.162,

Table 1
Causes of death for each CIx category.

	CIx 0	CIx I	CIx II	CIx III	CIx IV	Total
Malignancy	10 (23%)	9 (30%)	17 (21%)	14 (9.7%)	4 (3.7%)	54 (13%)
Endocrine	1 (2.3%)	2 (6.7%)	8 (9.8%)	6 (4.2%)	13 (12%)	30 (7.4%)
Dementia	2 (4.5%)	0 (0%)	3 (3.7%)	2 (1.4%)	11 (10%)	18 (4.4%)
Neurological	0 (0%)	0 (0%)	0 (0%)	2 (1.4%)	0 (0%)	2 (0.49%)
Cardiovascular	21 (48%)	13 (43%)	44 (54%)	95 (66%)	73 (67%)	246 (60%)
Pulmonary	1 (2.3%)	0 (0%)	6 (7.3%)	5 (3.5%)	1 (0.92%)	13 (3.2%)
Gastroenterological	3 (6.8%)	2 (6.7%)	1 (1.2%)	6 (4.2%)	3 (2.8%)	15 (3.6%)
Urological	1 (2.3%)	0 (0%)	0 (0%)	1 (0.69%)	1 (0.92%)	3 (0.73%)
Alcohol	3 (6.8%)	0 (0%)	0 (0%)	1 (0.69%)	0 (0%)	4 (0.97%)
Accident or violent	1 (2.3%)	3 (10%)	1 (1.2%)	9 (6.3%)	2 (1.8%)	16 (3.9%)
Not available	0 (0%)	0 (0%)	1 (1.2%)	0 (0%)	0 (0%)	1 (0.25%)
Miscellaneous	1 (2.3%)	1 (3.3%)	1 (1.2%)	3 (2.1%)	1 (0.92%)	7 (1.7%)
Death	44 (35%)	30 (43%)	82 (35%)	144 (50%)	109 (65%)	408 (46%)
Survive	82 (65%)	40 (57%)	153 (65%)	145 (50%)	58 (35%)	479 (64%)
Total	126	70	235	289	167	887

Distribution of causes of death varied significantly among CIx categories for endocrine ($p = 0.035$), dementia-related ($p < 0.001$) and cardiovascular ($p < 0.001$) causes of death.

Fig. 2. Kaplan-Meier curves show the cumulative survival for a 7-year follow-up.
Curves for Crural Index I-IV and no observable atherosclerosis in crural vessels (CI 0). Left side of the panel: mean estimated survival. (A) Cardiovascular survival and (B) overall survival.

Confidence interval (CI) 95% 1.23–3.80, $p = 0.007$) and CIx IV (HR 3.513, 95% CI 1.93–6.41, $p < 0.001$) were associated with a significant risk in a Cox regression model including high TBI (HR 0.137, 95% CI 0.056–0.333, $p < 0.001$) as a confounding factor. In addition, baseline variables including CAD (HR 1.435, 95% CI 1.08–1.91, $p = 0.013$), history of smoking (HR 0.597, 95% CI 0.403–0.884, $p = 0.010$) and age (HR 0.975, 95% CI 0.962–0.989, $p < 0.001$) were also associated with a significantly differing risk of death. Table 3 shows the results of Cox regression analyses. Separate models are shown for cardiovascular death and overall death with either ABI or TBI as confounding factors.

For overall mortality, CIx IV was significantly associated with mortality (HR 2.357, 95% CI 1.68–3.83, $p < 0.001$) in a Cox regression model including TBI (HR 0.208, 95% CI 0.105–0.41, $p < 0.001$) as a confounding factor (Table 3).

3.5. Most severely affected arterial segment and mortality

The risk of cardiovascular mortality was significantly increased when the crural segment was the most severely affected arterial segment (HR 2.321, 95% CI 1.45–3.73, $p < 0.001$) in a Cox regression model including high TBI as a confounding factor (HR 0.092, 95% CI

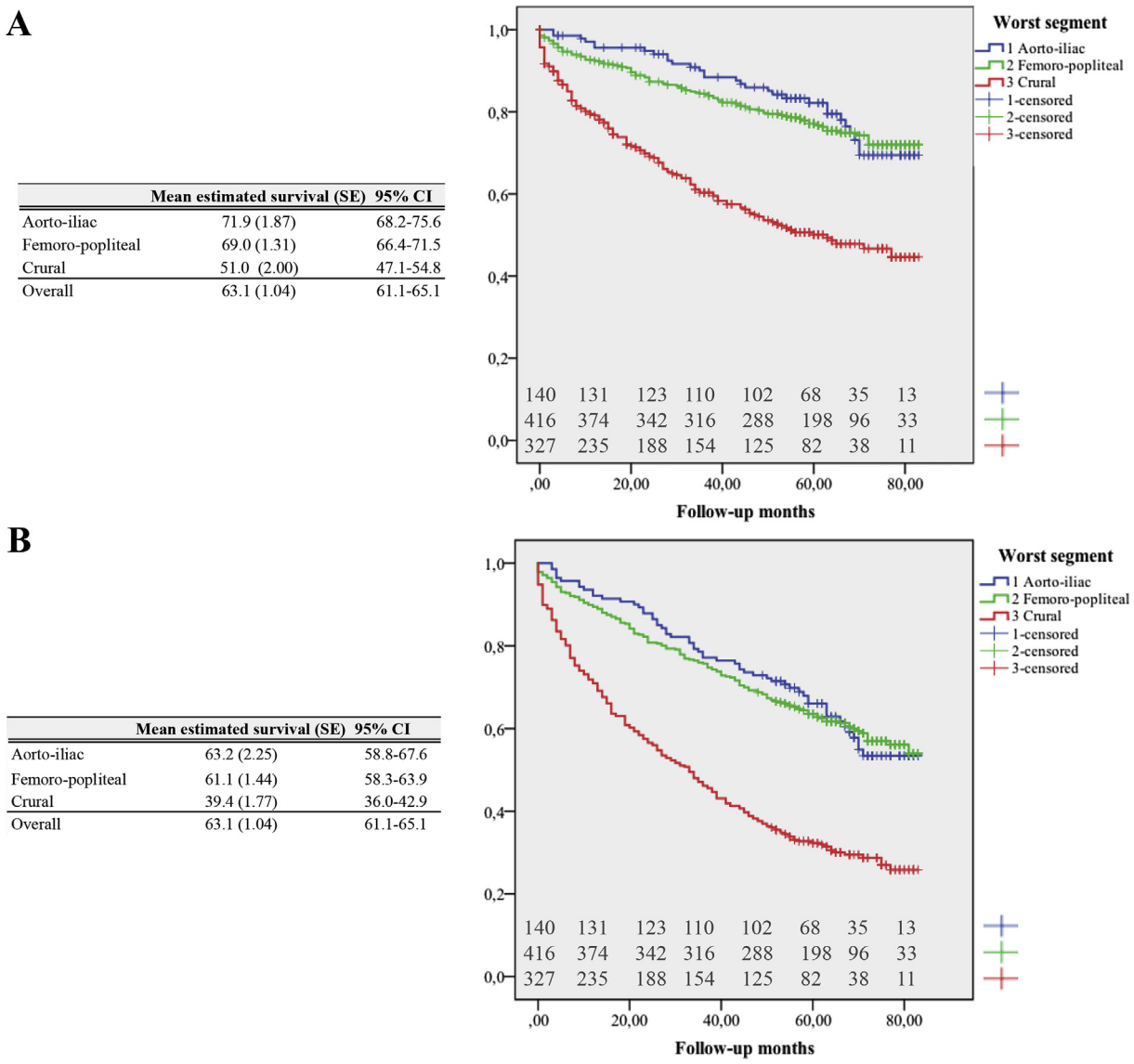

Fig. 3. Kaplan-Meier curves show the cumulative survival for a 7-year follow.
Curves for the most severely affected vascular segment. Left side of the panel: mean estimated survival. (A) Cardiovascular survival and (B) overall survival.

Table 3
Association between extent of crural vessel atherosclerosis, cardiovascular survival, overall survival and prognosis.

	Model A cardiovascular death TBI			Model B cardiovascular death ABI		
	HR	95% CI	*p* value	HR	95% CI	*p* value
CIx IV	3.513	1.93–6.41	<0.001	4.565	2.53–8.24	<0.001
CIx III	2.162	1.23–3.80	0.007	2.402	1.37–4.21	0.002
CIx II	1.618	0.909–2.88	0.102	1.571	0.881–2.80	0.126
CIx I	1.605	0.764–3.37	0.212	1.321	0.630–2.77	0.461
CIx 0	Reference			Reference		
	Model C overall death TBI			Model D overall death ABI		
	HR	95% CI	*p* value	HR	95% CI	*p* value
CIx IV	2.537	1.68–3.83	<0.001	3.282	2.19–4.92	<0.001
CIx III	1.395	0.952–2.05	0.088	1.557	1.06–2.29	0.024
CIx II	1.171	0.796–1.72	0.422	1.179	0.798–1.74	0.408
CIx I	1.138	0.676–1.92	0.626	1.019	0.608–1.71	0.944
CIx 0	Reference			Reference		

CIx 0 and confounding factors for both cardiovascular and overall Cox regression analyses according to univariate analyses as described in Results. Model A and C TBI and model B and D ABI.

0.039–0.222, $p < 0.001$). The following baseline variables forced into the model were associated with a significantly different risk of death: CAD (HR 1.517, 95% CI 1.14–2.01, $p = 0.004$), history of smoking (HR 0.592, 95% CI 0.401–0.873, $p = 0.008$) and age (HR 0.979, 95% CI 0.966–0.992, $p = 0.002$).

Crural vessels as the most severely affected arterial segment was associated with a significantly increased risk of overall mortality (HR 2.177, 95% CI 1.53–3.10, $p < 0.001$) in a model with high TBI (HR 0.152, 95% CI 0.078–0.295, $p < 0.001$) as a confounding factor. Table 4 shows the results of multivariate analysis.

4. Discussion

Classifications of lower extremity PAD using angiographic analysis have been described [10–13], but these classifications aim to guide the choice of treatment modality or to classify the severity of atherosclerosis. CIx was recently shown to associate with significant mid-term (up to three years) mortality and amputation at its higher categories III-IV [17,18]. Observations of the same cohort

Table 4
Association between the most severely affected lower limb arterial segment, cardiovascular survival, overall survival and prognosis.

	Model A cardiovascular death TBI			Model B cardiovascular death ABI		
	HR	95% CI	*p* value	HR	95% CI	*p* value
Crural	2.321	1.45–3.73	<0.001	2.578	1.61–4.11	<0.001
Femoro-popliteal	1.003	0.635–1.58	0.990	1.030	0.657–1.61	0.898
Aorto-iliac	Reference			Reference		
	Model C overall death TBI			Model D overall death ABI		
	HR	95% CI	*p* value	HR	95% CI	*p* value
Crural	2.177	1.53–3.10	<0.001	2.473	1.74–3.52	<0.001
Femoro-popliteal	0.944	0.657–1.32	0.737	1.000	0.716–1.40	0.999
Aorto-iliac	Reference			Reference		

Reference aorto-iliac segment and confounding factors for both cardiovascular and overall Cox regression analyses according to univariate analyses as described in Results. Model A and C: TBI; model B and D: ABI.

at up to 7-year follow-up are in accordance with earlier observations, showing that both cardiovascular and over-all mortality at CIx categories III and IV increase even further during long-term follow-up, compared to lower categories.

Significant atherosclerotic lesions at aorto-iliac or femoro-popliteal segments are associated with mortality [15]. Hemodynamically significant aorto-iliac lesions in particular have been shown to be associated with an increased risk of major adverse cardiovascular and cerebrovascular events (MACCE) [15,16,20]. Crural atherosclerosis has, controversially, been reported to both have no effect on survival [16] and to predict poor survival [20,21]. PAD patients with isolated crural disease have previously been shown to have poorer life expectancy compared to patients with multilevel disease, even if the multilevel disease involves the crural arteries [20]. In addition, an extensive study, utilising non-invasive screening of atherosclerosis at three segments of lower limb vascular beds, demonstrated that distal atherosclerosis is prognostic for poor survival [21]. There is still some controversy about the consequences of disease localisation and patient outcome in the literature. However, no earlier studies showing a correlation between the level of lower limb atherosclerosis and survival have focused on the possible value of the extent of atherosclerosis in lower extremity arteries. Our observations further support the idea that extensive atherosclerosis in crural arteries is associated with remarkably poor patient outcome, additionally highlighting the pronounced proportion of cardiovascular deaths among patients with CIx III-IV (66%). This emphasises the impact of a heavy burden of generalised atherosclerosis and cardiovascular disease in patients with a high CIx, as well as the importance of implementing the best available medical treatment for all PAD patients.

Clinical determination of causes of death and possible inaccuracies of death certificates are potential sources of significant error for a study such as this one. Although Finland has the highest autopsy rates of the Nordic countries (http://www.stat.fi/til/ksyyt/2013/ksyyt_2013_2014-12-30_laa_001_en.html), known PAD may in particular exaggerate the proportion of cardiovascular causes of death, in death certificates within the study population, which might render comparisons to the general population inaccurate. Within the study population of symptomatic PAD patients, however, this bias is likely to affect all patient groups in a similar manner, with a substantial 24% difference in cardiovascular mortality between patients with CIx I and CIx IV adding weight to the significance of this finding.

The clinical significance of crural vessel atherosclerosis is not limited to poor life expectancy alone. Isolated tibial disease is also associated with worse outcomes after revascularisation, even when compared to multilevel disease [22]. Our earlier [17,18] and present observations of CIx, together with an interesting investigation demonstrating that poor runoff is predictive of poor patient survival [14], uphold that the extent of crural atherosclerosis is predictive for both revascularisation outcome and patient survival. Whether the newly applied classification (WIfI) for severity of ischaemic ulcers will be predictive pf patient survival remains an interesting target for future research, as does the association of WIfI with runoff or CIx [23,24].

Aorto-iliac calcification and atherosclerotic lesions have been shown to be associated with poor patient outcome, defined as MACCE or death [16]. Our results demonstrate a 30% mortality among patients with the aorto-iliac segment most severely affected, but a 63% mortality among patients with severe crural segment disease. The severity and extent of atherosclerosis at the aorto-iliac segment in the present study are based on the TASC II classification and not on a simple yes/no evaluation of atherosclerosis at any given segment. This might explain different results between the present study and earlier observations. In previous studies, outcome was measured by MACCE as well as survival [16], not cardiovascular and overall mortality. According to our results, extensive atherosclerosis of crural arteries is associated with the worst patient outcome.

Aetiological differences between large and small vessel PAD have previously been characterised, with current smoking and dyslipidaemia in particular being associated with large vessel disease and diabetes with small vessel disease [25]. This can be considered to be in line with the findings in our study, where a positive smoking history was rare in patients with predominantly crural disease (9%) compared to those with aorto-iliac or femoro-popliteal disease (52 and 32%, respectively) [18]. Diabetes was similarly relatively rare (23%) in patients with predominantly aorto-iliac disease, as compared to those with femoro-popliteal or crural disease (41 and 53%, respectively). In fact, in the present cohort, smoking was associated with decreased cardiovascular mortality. This might be due to early smoking related deaths, such as those caused by malignancies, among smokers [26], and typical onset of symptomatic PAD at an older age [27] [18].

Co-morbidities in the present study are similar to those found in earlier studies on PAD [4,28–30]. End-stage renal disease and diabetes are associated with crural PAD [31–34]. Furthermore, these risk factors, together with critical ischemia, are shown to be associated with a poor prognosis [20]. Based on our observations, mortality correlates with the extent of atherosclerosis in crural vessels. The three most common causes of death during follow-up in the study cohort were cardiovascular (60%), malignancy (13.2%) and endocrine (7.3%). All baseline variables considered, extensive crural atherosclerosis measured as CIx is the strongest independent predictor of cardiovascular and overall mortality.

The aim of this study was to verify the association of the Crural Index with both cardiovascular and overall mortality during a long follow-up of up to 7 years. CIx is feasible in everyday vascular

practice and is a good indicator of patient outcome. It is applicable to assess patient mid-term [17,18] and long-term survival among patients with PAD. CIx may be valuable when making decisions on extensive, high-risk revascularisations for patients with multiple comorbidities.

Conflict of interest

The authors declared they do not have anything to disclose regarding conflict of interest with respect to this manuscript.

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